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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,538	07/10/2006	Yaeta Endo	20080-00002	7724

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,538	ENDO ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 19-21* is/are pending in the application.

4a) Of the above claim(s) *3,4,8 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-7,9,10,16,17 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 18 and 22-24 have been canceled. Claims 1-17 and 19-21 are at issue and are present for examination.

Applicant's election with traverse of Group II, claims 1, 2, 5-7, 9, 10, 16, 17, and 19-21 in the reply filed on 4/13/09 is acknowledged. The traversal is on the ground(s) that there would not be an undue burden for the coexamination of all groups as all are drawn to the concept of preparing cell extracts for use in translation systems. This is not found persuasive because each of the groups will require a separate search focusing on the different components of the cell to be removed or modified and knowledge regarding the interaction of each such component with the translation machinery. The requirement is still deemed proper and is therefore made FINAL.

Claims 3, 4, 8, 11-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/13/09.

Claims 1, 2, 5, 6, 9, 10, and 19-21 are objected to as including non-elected subject matter.

The disclosure is objected to because of the following informalities: the brief description of the drawings is placed following the examples instead of prior to the detailed

description of the invention. Appropriate correction is required.

Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 10 are confusing in the recitation of "fractional elimination of molecular weight" as molecular weight is a property of a compound which cannot be separated from the compound. It is assumed applicants intended "fractional elimination of low molecular weight compounds"

Claims 1, 2, 5, 6, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of preparing a genus of *in vitro* protein synthesis systems and a genus of *in vitro* protein synthesis systems which comprise a genus of cell extracts having reduced activity of any cell derived mechanism for inhibition of translation or elimination of any means of

controlling a ATP-mediated sugar phosphorylation system. The specification teaches only a single representative species of such cell extracts, i.e., a cell extract in which low molecular weight compounds have been removed by fractionation by gel filtration and/or ultrafiltration. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having reduced activity of any cell derived mechanism for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system. Protein synthesis and sugar phosphorylation are highly complex and in many respects poorly understood cellular systems involving many interrelated cellular factors such that alterations of these pathways may produce many unpredictable effects. The specification fails to describe other means of achieving the functional feature of elimination of any cell derived mechanism for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system beyond a recitation of modulating some known components of at least some such systems. However, there is absolutely no supporting evidence that any of these various means would actually be successful and the effects of doing most of these are entirely unpredictable. For example the specification

recites removing phosphorylated sugars from the cell extract as a means of controlling a ATP-mediated sugar phosphorylation system. However, the examples presented in the specification suggest that the inhibitory effects of monosaccharides within *in vitro* translation systems is a result of the utilization of available energy supplies, particularly ATP, for the phosphorylation of the monosaccharides. If this is in fact what is occurring then selective removal of phosphorylated sugars from the extract is likely to in fact accelerate this inhibitory reaction not inhibit it as phosphorylated sugars are the product of the inhibitory reaction and removal of the product will tend to shift the equilibrium of this reaction further toward production of the product. Similarly applicants specification recites removing or inhibiting glycolytic enzymes as a means of controlling a ATP-mediated sugar phosphorylation system. However, some glycolytic enzymes are clearly necessary for activity of most *in vitro* protein synthesis systems as the standard energy sources for such systems are in fact glycolytic intermediates and thus require the presence of those glycolytic enzymes which produce ATP from these compounds. For all the above reasons the specification fails to describe the enormous breath of elimination of any cell derived mechanism for

inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system.

Claims 1, 2, 5, 6, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of preparing an *in vitro* protein synthesis system in which low molecular weight compounds have been removed by fractionation by gel filtration and/or ultrafiltration or in which glucose and/or other monosaccharides have been removed and *in vitro* protein synthesis systems prepared by these methods, does not reasonably provide enablement for methods of preparing any *in vitro* protein synthesis system having reduced activity of any cell derived mechanism for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system and any *in vitro* protein synthesis systems prepared by these methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

These claims are directed to methods of preparing a genus of *in vitro* protein synthesis systems and a genus of *in vitro* protein synthesis systems which comprise a genus of cell extracts having reduced activity of any cell derived mechanism

for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system. However the specification each only a very limited number of such extracts or cell derived mechanisms for inhibition of translation or means of controlling a ATP-mediated sugar phosphorylation system. Protein synthesis and sugar phosphorylation are highly complex and in many respects poorly understood cellular systems involving many interrelated cellular factors such that alterations of these pathways may produce many unpredictable effects. The specification fails to describe other means of achieving the functional feature of elimination of any cell derived mechanism for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system beyond a recitation of modulating some known components of at least some such systems. However, there is absolutely no supporting evidence that any of these various means would actually be successful and the effects of doing most of these are entirely unpredictable. For example the specification recites removing phosphorylated sugars from the cell extract as a means of controlling a ATP-mediated sugar phosphorylation system. However, the examples presented in the specification suggest that the inhibitory effects of monosaccharides within *in vitro* translation systems is a result

of the utilization of available energy supplies, particularly ATP, for the phosphorylation of the monosaccharides. If this is in fact what is occurring then selective removal of phosphorylated sugars from the extract is likely to in fact accelerate this inhibitory reaction not inhibit it as phosphorylated sugars are the product of the inhibitory reaction and removal of the product will tend to shift the equilibrium of this reaction further toward production of the product. Similarly applicants specification recites removing or inhibiting glycolytic enzymes as a means of controlling a ATP-mediated sugar phosphorylation system. However, some glycolytic enzymes are clearly necessary for activity of most *in vitro* protein synthesis systems as the standard energy sources for such systems are in fact glycolytic intermediates and thus require the presence of those glycolytic enzymes which produce ATP from these compounds. The specification provides little guidance for the selection of those inhibitors/cell extracts which can be successfully used from those which cannot. Furthermore, the specification provides virtually no guidance for the skilled artisan with regard to making the enormous scope of cell extracts encompassed by the instant claims. Producing a cell extract with reduced activity of any protein requires detailed knowledge of the structure of the genes encoding that

protein and/or methods of regulating the activity of the specific protein of interest. As such production and use of the entire scope of *in vitro* protein synthesis systems claimed would be well beyond the bounds of routine experimentation. For all the above reasons the specification fails to enable the enormous breath of elimination of any cell derived mechanism for inhibition of translation or elimination of any means of controlling a ATP-mediated sugar phosphorylation system.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-7, 9, 16, 17 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Endo (WO 03/064672, see US PGPUB 2005/0064592 for an English translation thereof). Note all reference citations herein refer to the corresponding US Patent Application Publication not the WO document.

Endo teach methods for preparing cell extracts for use as cell free protein synthesis systems comprising elimination of cell derived low molecular weight substances that inhibit protein synthesis (see paragraph [0012]). Endo specifically teach that the cell free protein synthesis systems can be

prepared from any known protein synthesis cell extract including those from *E. coli*, plant cell embryos and rabbit reticulocytes (see paragraph [0042]). Endo teach that specifically substance having molecular weights below 14,000 daltons should be removed (see paragraph [0014]) and that such substances can be removed by methods comprising dialysis, gel filtration, and ultrafiltration (see paragraph [0062]). While Endo do not specifically teach the removal of glucose and/or other monosaccharides, these compounds are inherently removed by fractionation by the methods taught by Endo to remove compounds having molecular weights below 14,000 daltons and the extracts prepared by Endo inherently have a glucose concentration of less than 10 mM or less.

Claims 1, 2, 6, 7, 9, 10, 6, 17, and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yao et al.

Yao et al. teach methods of preparing wheat germ protein synthesis extracts comprising preparing a wheat germ extract wherein preparation of the extract includes a step of gel filtration on Sephadex G-25 and an ultrafiltration step with a ultrafiltration disk having a 30kDa cut off. (see page 549). While Yao et al. do not specifically teach the removal of glucose and/or other monosaccharides, these compounds are inherently removed by fractionation by the methods taught by Yao

et al. and the extracts prepared by Yao et al. inherently have a glucose concentration of less than 10 mM or less.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-7, 9, 10, 16, 17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Endo (WO 03/064672).

Endo is discussed above but does not specifically teach using repeated steps of ultrafiltration or gel filtration. However a skilled artisan would readily understand the repeating the ultrafiltration or gel filtration would assure complete removal of the low molecular weight inhibitors. Therefore, it would have been obvious to one of ordinary skill in the art to

use multiple rounds of ultrafiltration or gel filtration to remove the low molecular weight inhibitory compounds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652